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EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

EUnetHTA 21

Guidance Document

D7.1 – Practical Guideline for interaction between Health Technology Developer and HTA bodies

Version 0.1, 22.04.2022

Template version 1.0, October 2021

Document history and contributors

Version	Date	Description
V0.1	22/04/2022	First draft
V0.2	22/06/2022	Second draft
V0.3	20/07/2022	For Public consultation

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This Guidance document was produced under the Third EU Health Programme through a service contract with the European Health and Digital Executive Agency (HaDEA) acting under the mandate from the European Commission. The information and views set out in this guidance document are those of the author(s) and do not necessarily reflect the official opinion of the Commission/ Executive Agency. The Commission/Executive Agency do not guarantee the accuracy of the data included in this study. Neither the Commission /Executive Agency nor any person acting on the Commission's / Executive Agency's behalf may be held responsible for the use which may be made of the information contained therein.

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The work in EUnetHTA 21 is a collaborative effort. While the agencies in the Hands-on Group will be actively writing the deliverable, the entire EUnetHTA 21 consortium is involved in its production throughout various stages. This means that the Committee for Scientific Consistency and Quality (CSCQ) will review and discuss several drafts of the deliverable prior to validation. Afterwards the Consortium Executive Board (CEB) will endorse the final deliverable prior to publication.

External Stakeholder Contribution

To be completed after public consultation.

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List of abbreviations

CEB	Consortium Executive Board
CHMP	Committee for Medicinal Products for Human Use
CSCQ	Committee for Scientific Consistency and Quality
EUnetHTA	European Network of Health Technology Assessment
F2F Meeting	Face to face meeting/ meeting with the HTD (and EMA) during JSC
HTA	Health Technology Assessment
HTAb	HTA bodies
HTAR	EU HTA Regulation – Regulation (EU) 2021/2282
HTD	Health Technology Developer
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
LoMI	List of Missing Items
MS	Member State
SOP	Standard Operating Procedure

1 GENERAL PRINCIPLES AND PURPOSE

1.1 General principles

During Joint Action 3 (JA3) procedures have been developed and tested regarding the interaction between Health Technology Developers (HTD) and Health Technology Assessment bodies (HTAb). When defining procedures for future interaction between HTD and HTAb, it is important to ensure the independence of the Joint Clinical Assessments (JCA) and Joint Scientific Consultations (JSC) assessment teams. It also is important to ensure procedurally fair processes for HTD. In addition, it is important that the procedures are in line with the steps outlined in the Health Technology Assessment Regulation (EU) 2021/2282 (hereafter referred to as HTAR).

While this guidance follows the requirements as set out in the HTAR, the HTAR is not yet applied, therefore the EUnetHTA 21 Service Contract does not follow the same legal framework as the HTAR. This means that activities (JCA and JSC) carried out within EUnetHTA 21 may have a more interactive process with the HTD than the JCA and JSC carried out under the HTAR. Therefore, this guidance document describes in some cases the process for EUnetHTA 21 and the recommended process for under the HTAR. Chapter 3 will explain this in more detail.

1.2 Purpose and Scope

This document defines the objective and extent of any formal interaction between HTAb and HTD for JCA and JSC, based on requirements set out in the HTAR and experiences from EUnetHTA Joint Action 3.

This document does not describe the interaction with HTD as a stakeholder for EUnetHTA 21 deliverables, this is described in a separate SOP.

During EUnetHTA 21, more interaction with HTDs may take place than what is foreseen in the HTAR, due to the fact that the HTAR is not into force yet.

1.3 Relevant articles in Regulation (EU) 2021/2282

The HTAR specifies in a number of recitals and articles the interaction between HTD and HTA bodies. Table 1-1 shows which of these HTAR recitals and articles refer to JSC and/or JCA and in what stage of the production. For a complete overview, see Appendix 1.

Table 1-1: Recitals and articles of the HTAR referring to interaction between HTD and HTA

JSC	
Selection of Health Technologies for JSC	Art 17 (1), (2): HTD may request JSC Art 17 (4): inform HTD about selection
Submission of information by HTD	Art 18 (2): submission of information by JSC
Conduct of JSC	Art 16 (1) and Art 18 (7): meeting with HTD during JSC
Share outcome of JSC with HTD	Art 19 (2), Art 30 (1c)
JCA	
Selection of Health Technologies for JCA/CA	Art 7 (1): Health Technologies subject to a JCA Art 8: Initiation of a JCA
Scoping process	Recital 25: inclusive scoping process Art 8 (6): Consider HTD input on PICO Art 10 (1): Inform HTD about final PICO & request submission dossier

Submission dossier	Recital 36: timeframe for JCA and deadline for submitting data Art 10 (2) (5), (6), (8): - Submitting of dossier - Check for completeness & inform HTD about continuation or discontinuation
Assessment process	Recital 36: timeframe for JCA production Art 11 (2): Interaction with HTD in case clarifying questions during JCA Art 11 (5): - Factual accuracy check by HTD of draft JCA report - HTD to flag which sections are confidential
Publication of JCA/CA	Art 12 (4): Inform HTD about publication final JCA
Secure system for data sharing	Art 30 (1c)

2 ACTORS AND THEIR SCOPE

2.1 HTA bodies

HTAb are responsible for conducting the JSC and JCA work. Therefore, this term refers to the JSC and JCA Assessor and Co-Assessor, Secretariat, the members of the Committee for Scientific Consistency and Quality (CSCQ), and the Consortium Executive Board (CEB).

The Secretariat is responsible for all external communication, to ensure the independence of the Assessor and Co-Assessor. HTAb Assessor and Co-Assessor should have no direct interaction with the HTD. Should the HTD reach out to them directly with questions on the EUnetHTA 21 JCA or JSC, the Assessor and Co-Assessor should direct them to the Secretariat.

2.2 HTD

For JCA, the HTD is requested to follow the *JCA manual for HTD*[1]. In summary, the HTD is requested to inform the Secretariat about the claimed indication and a contact person (in EUnetHTA 21 this happens with the submission of a Letter of Intent), provide a submission dossier following the consolidated PICO(s) (Population, Intervention, Comparator(s) and Outcome(s)), join the PICO information meeting (only for EUnetHTA 21), and perform a factual accuracy check of the draft JCA report validated by the CSCQ. In EUnetHTA 21, the HTD is requested to provide timely information and status updates on the regulatory process, challenges and potential deviations in the regulatory timetable.

For JSC, the HTD is requested to follow the *JSC procedural guidance* published on EUnetHTA 21 and EMA websites[2].

The HTD is not allowed to communicate directly with Assessors and/or Co-Assessors of JCA or JSC, nor interact with other HTAb about the ongoing JCA or JSC on a European level unless it is publicly available information.

For JSC, national consultations must be requested directly from the Member State (MS). A national consultation should complement and/or address context-specific issues related to the national HTA

[1] This document is under develoSecretariatent. It most likely will follow a similar structure as the industry procedure manual developed in Joint Action 3, but of course the content will be updated to reflect the requirements from the HTAR and the EUnetHTA 21 deliverables.

[2] https://www.eunethta.eu/wp-content/uploads/2021/11/Guidance-on-parallel-consultation.pdf?x69613&x16454

system of the specific MS (see also Article 16 (4) HTAR). Duplicated full scientific consultations at the national level (similar questions for the JSC and the national advice) are not foreseen according to the HTAR provisions. Clarification meetings on the national positions are exempted but should not re-address agreed on positions. When requesting a national consultation, the HTD must inform HTAb about the JSC/JCA that have taken place or are ongoing on a European level.

3 RULES OF THE COLLABORATION

3.1 Confidentiality

There will be no confidentiality agreement between the participating HTD and EUnetHTA 21, neither for a JSC process, nor for a JCA.

Detailed rules on confidentiality of submitted information by the HTD, are described in the process for commercially sensitive and academic-in confidence data (part of D7.1 documents – to be hyperlinked when available). Further information about the confidentiality, publication and citation policy of the submission dossier for a JCA can be found in the submission dossier requirements. The final submission dossier is published, together with the final JCA report.

3.2 Status of Outputs

For JCA, the HTD should follow the JCA Manual for HTD. This manual is binding and describes which (version of the) tools, templates, guidelines etc. are to be used during the JCA. The manual will be shared with the HTD after they submitted their Letter of Intent and once they have been accepted for a JCA in EUnetHTA 21.

Once a Letter of Intent is submitted and the Health Technology is accepted by EUnetHTA 21 for a JSC or JCA, the process officially starts. As soon as the HTD has submitted their draft briefing book (for JSC) or the submission dossier (for JCA), the process cannot be terminated by the HTD. This means the documents submitted by the HTD cannot be withdrawn and the JCA/CA or JSC process will continue also with publication of documents as required for the JCA/CA or JSC procedure. However, the HTD should inform EUnetHTA 21 about any changes in the develoSecretariatent plans that might have impact on the ongoing JSC or JCA. In the event the HTD withdraws the product from the regulatory marketing authorisation process, if the HTD goes bankrupt or in case there is a negative outcome of the regulatory process, the JCA will be discontinued. In such event, there is no final JCA report and thus the submission dossier will not be published, however, the consolidated PICO will be published. For a JSC, Only aggregated generic information on JSC can be content of an JCA report, e.g. whether the HTD deviated from the common recommendation of the JSC. No information on product specific questions or national specifications nor the complete content of an advice can be published.

For EUnetHTA 21, all documents submitted by the HTD, are stored internally on the respective SharePoint page which all CSCQ members, appointed participants and Assessor and Co-Assessors have access to. For JCA, the CEB members will also have access to the documents submitted. For JSC, only the CSCQ members will have access.

If, for JCA in EUnetHTA 21, a PICO information meeting is held, such a meeting only serves the purpose to inform the HTD about the consolidated PICO(s), and there is no provision to alter the PICO(s) at this point and no final decisions will be taken during the PICO information meeting. No minutes will be published or shared with the HTD after the meeting, nor will the meeting be recorded. See section 4.2.1 for further details.

Both in EUnetHTA 21 as in the HTAR, the final submission dossier (for JCA) will be published together with the final JCA report. See D7.1.3 (guidance on handling confidential data) for further details. In

EUnetHTA 21, re-use of the final JCA report will not be mandatory at the national level but is encouraged whenever possible.

Both in EUnetHTA 21 as in the HTAR, comments provided by the HTD during a factual accuracy check of the final draft JCA report will be made publicly available, together with the Assessor and Co-Assessor answers to the comments, once the final JCA report is published. The process for a factual accuracy check is further detailed in the guidance document for factual accuracy check (part of the D7.1 documents – to be hyperlinked when available).

4 PROCESS

4.1 Joint Scientific Consultations

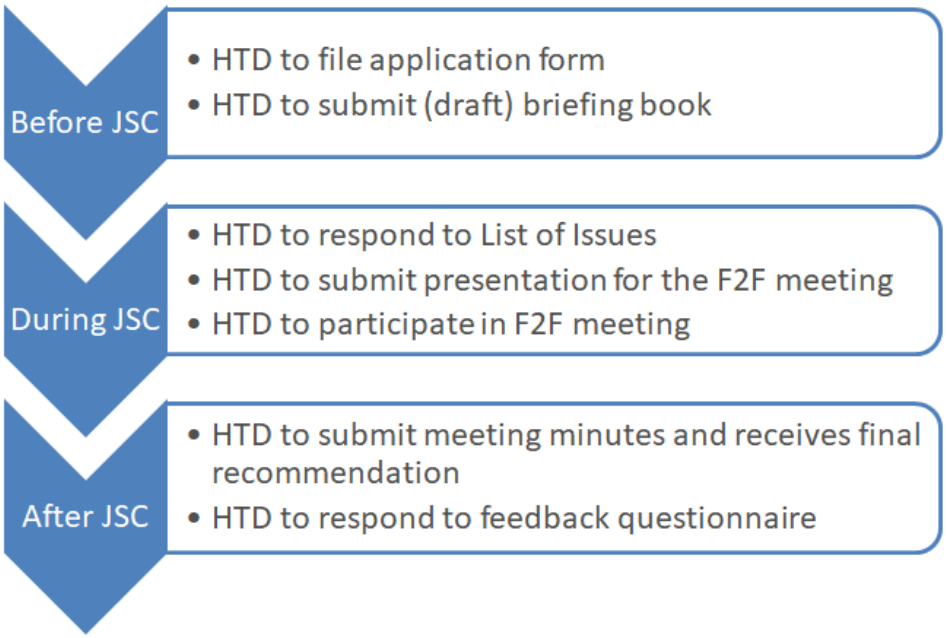

Figure 4-1: Process overview for JSC and Interaction between HTAb and HTD (for EUnetHTA 21 and HTAR)

4.1.1 HTAb and HTD interaction before JSC starts

Application for JSC

Under the HTAR, it is envisaged that the Coordination Group shall publish the dates of request periods and state the planned number of JSCs for each of those request periods on the IT platform referred to in Article 30. At the end of each request period, where the number of eligible requests exceeds the number of planned JSCs, the Coordination Group shall select the health technologies that are to be subject to JSCs, ensuring the equal treatment of requests concerning health technologies with similar intended indications. The criteria for selecting from eligible requests for medicinal products and medical devices are outlined in the HTAR (Art. 17 (3)).

Within EUnetHTA21, the CSCQ publish the dates of the request periods (Open Call for JSC) and state the planned number of JSCs for each of those request periods on the EUnetHTA website and via social media. Within the request period the HTD has to submit an application form (link on EUnetHTA website) to the JSC secretariat. The HTD receives a confirmation of receipt.

At the end of each request period, the CSCQ select eligible applications which will be subject to JSC. The criteria for selecting eligible requests are publicly available [3] and are based on the criteria outlined in the HTAR and supplemented with additional prioritisation criteria for EUnetHTA 21.

[3] https://www.eunethta.eu/jsc/

Selection of products for JSC

At the end of the request period and following selection of eligible products applying the selection criteria stated in the Open Call for JSC, HTDs will be informed by the JSC secretariat/ the Coordination group (for the HTA R) whether they were selected for JSC. Where a request for JSC was refused, the HTD will be informed thereof and the reasons explained.

Submission of the (draft) Briefing book and check for completeness

The HTD must submit the briefing book to the JSC secretariat according to the published timeline for the accepted time slot. The HTD receives a Written Request for Clarification if there are missing items in the draft Briefing book, e.g. explanations on the study design or missing supporting documents on endpoints. The Applicant sends the final version of the Briefing Book (a “track changes” version and a “clean” version) taking into consideration Written Requests for Clarification, if applicable.

4.1.2 HTAb and HTD interaction during JSC

List of issues

Approximately 30 days after submission of the final Briefing book the JSC secretariat will share the EUnetHTA 21 List of issues and the template for Applicant’s Written Response, with the HTD. The HTD has to provide all introduced changes in a table format and to provide answers to “Issues to be addressed in writing only” ato the JSC secretariat.

F2F - meeting

The HTD has to submit the slides that will be presented during the F2F meeting. . In case of any questions the JSC secretariat will give feedback on structure of the slides prior to the meeting if they need modification in structure to be suitable for the F2F meeting. The slides should follow the PICO scheme according to the Questions in the Briefing book and present the issues from the lists of issues of the HTAb and EMA to be addressed by the HTD during the F2F meeting. The HTD has to take meeting minutes.

4.1.3 HTAb and HTD interaction after JSC

The HTD sends the F2F meeting minutes to the JSC secretariat. The meeting minutes will only serve as a tool of record and will not be commented on by EUnetHTA 21, nor will they be included in the final recommendations.

Final recommendations

After the F2F meeting the HTD can expect the final written recommendations according to the timelines in the procedure for JSC.

Evaluation

Participating HTD in a JSC are encouraged to submit their feedback on the procedure throughout the JSC production. After finalisation of the JSC, a feedback survey is sent to HTD by the JSC Secretariat.

4.2 Joint Clinical Assessments

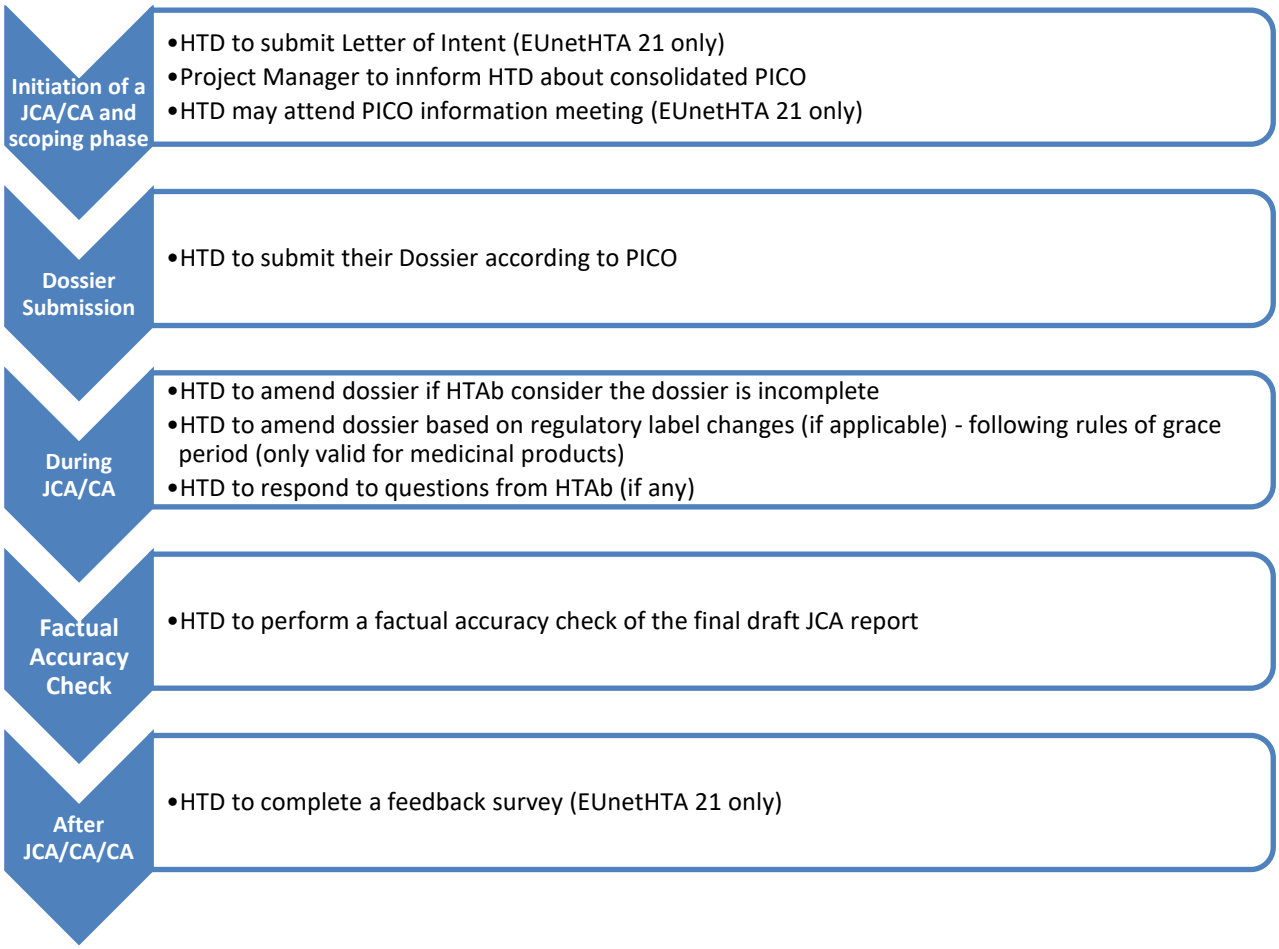

Figure 4-2: Process flow for JCA and interaction between HTAb and HTD (for EUnetHTA 21 and HTAR)

4.2.1 Initiation of a JCA and Scoping phase

Selection of Health Technologies for JCA

Under the HTAR, article 7 defines the health technologies eligible for a JCA. For medicinal products, there is no additional selection process under the HTAR. For more information on the operationalisation of the selection process for Medical Devices JCA, see deliverable D4.7.3 and D4.7.4.

During EUnetHTA 21, the HTD is expected to submit a signed Letter of Intent, in which they indicate their intent to participate in a JCA. Submission of a Letter of Intent does not automatically lead to acceptance of the technology for a JCA in EUnetHTA 21. The Secretariat will inform the HTD once their technology is accepted for a JCA in EUnetHTA 21.

In the Letter of Intent, the HTD is requested to state the contact person for the JCA process, the claimed indication and the anticipated regulatory pathway.

A Letter of Intent is not foreseen under the HTA Regulation.

Submission of PICO(s) & Request Submission Dossier

Both under the HTAR and EUnetHTA 21, as per Art 10 (1) of the HTAR, the Secretariat informs the HTD about the consolidated PICO(s) for the JCA and requests a completed submission dossier as per the

PICO(s) by a specified deadline. The HTD has to submit their JCA dossier, after the consolidated PICO(s) has been submitted to the HTD.

PICO information meeting (only EUnetHTA 21)

In the HTAR there is no meeting envisioned between the HTD and HTAb during or after the scoping process. In EUnetHTA 21, the HTD is invited to join a PICO information meeting, in which the assessor and co-assessor present the consolidated PICO(s). The purpose of this meeting is to provide the HTD with information on the consolidated PICO(s), and is not a meeting to discuss submission requirements. There is no provision to amend the EUnetHTA 21 consolidated PICO(s) at this point.

4.2.2 Submission Dossier for a JCA

Receipt of Submission Dossier & check of completeness

Both under the HTAR and EUnetHTA 21, the Assessor and Co-Assessor perform a technical completeness check within 10 calendar days upon receipt of the submission dossier and the Secretariat performs a procedural completeness check. The HTD has to submit a dossier according to the scope of the JCA (i.e. submit data or prove there is no data available for all identified PICO(s)), otherwise the dossier has to be declared incomplete. A list of missing items (LoMI) will be shared with the HTD by the end of this check. The time for providing the amended dossier responding to the LoMI depends on the JCA procedure (i.e. medicinal products or medical devices). The objective of the technical check of completeness is to ensure completeness of the dossier to avoid interaction (via Secretariat) between the HTD and the Assessor and Co-Assessor during the actual assessment.

The HTD has to make sure the consolidated PICO(s) are addressed in the submission dossier. In case of any deviations a sound justification must be provided.

In EUnetHTA 21, in case the HTD does not provide the amended Submission Dossier by the deadline, or the Submission Dossier is still considered incomplete by the Assessor and Co-Assessor, the Assessor and Co-Assessor will discuss with the CSCQ and CEB if they can proceed with the JCA or whether the JCA should be discontinued.

For medicinal products only: Although EUnetHTA 21 does not have clock-stops, a grace period to amend the Submission Dossier is allowed if CHMP opinion differs from what was anticipated and only to those sections impacted by the CHMP opinion. The need for and duration of a grace period has to be approved between the Assessor and Co-Assessor and the Secretariat, but can take a maximum of 10 calendar days (starting once CHMP opinion is available). During the grace period the Assessor and Co-Assessor will update the PICO, which will be published approximately 1 week after CHMP opinion.

Formal interaction with HTD during the JCA

As per Art. 11(2), interaction with the HTD should be possible at any time during preparation of the JCA in case the Assessor and Co-Assessor consider that further specifications or clarifications or additional information, data, analyses or other evidence are necessary in order to carry out the assessment. In this case, the Secretariat reaches out to the HTD with a formal request to provide such information, data, analyses or other evidence. Depending on the type of request, a deadline (with a maximum of 5 calendar days for medicinal products and 14 calendar days for MDs/IVDs) to provide the requested information will be communicated.

Both under the HTAR and EUnetHTA 21, according to art. 11(2), where new clinical data becomes available during the assessment process, the HTD concerned shall proactively inform the Coordination Group about this prior to the start of the JCA indicating anticipated timelines when it will become available. Within EUnetHTA 21, this means that the HTD shall inform the Secretariat.

The Secretariat is responsible for communicating any questions from the Assessor and Co-Assessor to the HTD, requesting the required input from the HTD and sharing the received input with the assessor and co-assessor.

There will be no direct contact between the HTD and the Assessor and/or Co-Assessor during the JCA, outside of the PICO information meeting.

4.2.3 Factual accuracy check of JCA by HTD

Art. 11(5) specifies that the draft JCA reports shall be provided to the HTD. Within EUnetHTA 21, the draft reports that will be shared are the drafts validated by the CSCQ. The HTD shall signal any purely technical or factual inaccuracies in accordance with the timeframes established pursuant to Article 15. For more information on the factual accuracy check, please see the document D7.1 Procedure and Framework for the Factual Accuracy Check

4.2.4 HTA and HTD interaction after JCA

Publication of a JCA

Once the final JCA report, submission dossier and answers/comments from the factual accuracy check are published, the Secretariat shares the link with the HTD.

Evaluation (EUnetHTA 21 only)

Participating HTD in a JCA are encouraged to submit their feedback on the procedure throughout the JCA production. After each JCA is finalised, a survey is sent to HTD

Error reporting procedure

In case potential errors are identified in a EUnetHTA 21 JCA report after its publication, EUnetHTA can start the error reporting procedure. The person reporting the error is requested to reach out to eunethta@zinl.nl, and state the following:

- Your affiliation and contact details;
- Specifically describe the potential error you discovered (mention the title of the report (and the project ID), state both the page number and the specific sentence, and mark the error);
- If applicable, please also submit a reference to a source where the correct information can be found.

More information can be found here.

5 PRACTICAL ISSUES

5.1 Contact Points (EUnetHTA 21 only)

The JCA Secretariat (JCA/CA_Secretariat@zinl.nl) is the primary point of contact for the HTD for JCA on medicinal products and medical devices.

The JSC Secretariat (EUnetHTA21-JSC@g-ba.de) is the primary point of contact for the HTD for JSC.

5.2 Other

A secure system will be used for data sharing between HTD and EUnetHTA 21, in the form of a secure e-mail system, Eudralink or through SharePoint.

6 CONSIDERATIONS FOR THE HTAR

- Appoint a dedicated Secretariat per JSC and JCA
- A secure data sharing system has to be used
- Use a JSC and JCA HTD manual, which explain the process and formal points for interaction between HTD and HTAb
- Use a tool to confirm and keep track of tools, templates, procedures and guidance that are applicable for the specific JSC and JCA
- Consider using a form by which the HTD can provide information on the following:
    - the contact person for the JCA process,
    - the claimed indication/intended use
    - the anticipated regulatory pathway and respective timelines
- Discuss if new evidence can be accepted during an ongoing JCA and if so, define a process for submission of this new evidence during an ongoing JCA